

REMARKS

Claims 1-23 had been previously canceled, without prejudice.

Claims 24-33 are canceled in this submission, without prejudice.

As indicated in the Advisory Action mailed August 19, 2003, the amendment proposed in Applicants' August 4, 2003 submission had not been entered. Applicants request that the August 4, 2003 amendment NOT to be entered. Hence, claim 34 remain un-entered.

New claims 35-37 have been added and are currently pending.

No new matter has been added. The new claims are fully supported by the original specification. Specifically, attached Table A summarizes support for the amino acid side chains (R₁, R₂ and/or R₃); attached Table B summarizes support for the tether (T); attached Table C summarizes support for Y; and attached Table D summarizes support for the protecting groups on amino acid side chains (W).

Entry of this amendment is respectfully requested, as it is believed to place the claims in condition for allowance.

Change of Inventorship

Applicants acknowledge the Examiner's confirmation that all requirements for amendment of the inventorship have been fulfilled and that Luc Ouellet and Ruoxi Lan have been withdrawn as inventors.

Priority

Applicants also acknowledge that Canadian Patent Application No. 2,294,459 has been confirmed as affording a priority date of October 4, 1999 for the present application.

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Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 24-33 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter not supported by the specification. The Examiner states that this is a written description rejection.

Claims 24-33 have been canceled. Therefore, this rejection is rendered moot as to those claims.

New claims 35-37 have been added. It is respectfully submitted that claims 35-37 comply with the written description requirement of 35 U.S.C. § 112, first paragraph.

The subject matter of new claims 35 and 36 are similar to canceled claim 24, but claims 35 and 36 are limited to protected and deprotected tethered tripeptides. Claim 37 is narrower than claim 35 because claim 37 is directed to deprotected tethered tripeptides only. As stated above, the support for the new claims is detailed in attached Tables A-D.

Specifically, claims 35-36 call for a macrocyclic compound made of a tripeptidomimetic backbone defined by formula (1). This tripeptidomimetic backbone comprises three amino acid fragments (A1, A2, and A3) and a linker, herein called a tether (T). The tether is used as a linker between fragments A1 and A3 of the tripeptidomimetic backbone. The amino group on fragment A1 bears a radical Y, which can be either hydrogen or a protective group. Fragments A1, A2 and A3 can additionally be amino acids with side chains (R_1 , R_2 , or R_3), these side chains are either protected or deprotected (radicals W_1 to W_{16}).

Claim 36 is concerned with specific embodiments of radicals W_1 to W_{16} .

Claim 37 is directed to deprotected tethered tripeptides only.

Reference to the specification establishes that claims 35 and 36 satisfy the written description requirement. A person of ordinary skill in the art (in this case, a Ph.D. in synthetic organic chemistry) having reviewed the specification would readily conclude that the present inventors were in possession of the compounds of claims 35 and 36.

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The specific features and substituents of the compounds are expressly defined by the structural formula in claims 35 and 36. For example, the amino acid fragments are specifically identified at pages 6 and 7, and in Figure 1; the tethers are described at page 38, lines 6-12, and in Figure 1. For further clarity, attached Tables A and B identify the portions of the specification that specifically disclose the amino acids and tethers called for in claims 35-37. Table C identifies the portion of the specification where support can be found for radical Y and Table D lists specific examples of support for protected amino acid side chains (W_1 to W_{16}).

The specification discloses representative examples of the claimed macrocyclic tripeptides (see, for example, pp. 25-27, Tables 1-3; and pp. 35-37, Tables 4-6). These examples constitute a representative cross-section of the compounds called for in the general formula set forth in claim 34. The Examiner has acknowledged (on page 5 of the Final Office Action) that examples of tethered tripeptides are set forth in the specification.

As the Examiner will note, the protecting groups on the amino acid side chains are defined in claim 35 as " W_1 to W_{16} are protecting groups used for orthogonal protection in peptide synthesis". The expression "orthogonal protection" was used in cancelled claim 2. A person skilled in the art would understand that this expression is used to describe the fact two different protecting groups can be differentially removed by using specific reaction conditions. Claim 36 is an independent claim that lists specific groups for W_1 to W_{16} but does not contain the "orthogonal protection" language.

Additionally, the specification discloses methods of preparing several of the claimed compounds (see, for example, p. 33, line 23 to p. 37, line 7). These methods of preparation include detailed processing steps, such as particular reagents, filtrations, washes, and reaction times (see, for example, p. 34, line 21 to p. 35, line 5).

In *University of California v. Eli Lilly and Co.* ([CA FC] 43 USPQ2d 1398) the court stated that "a description of a genus ... may be achieved by means of a recitation of a representative number of [species] ..., falling within the scope of the genus or of a

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recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus" (emphasis added). Here, the specification discloses a representative number of species that fall within the generic formula (see for example, pages 35-37 (Tables 4-6)) and also discloses representative examples of making the claimed compounds (see for example, page 20, line 8 to page 44, line 26).

A review of the representative examples and the methods of preparation disclosed in the present specification would lead one of ordinary skill in the art to conclude that the inventors were in possession of the compounds defined in claims 35-37 at the time the present application was filed.

Rejections Under 35 U.S.C. §112, First Paragraph (Enablement)

Claims 24-33 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter not supported by the specification. The Examiner states that this is an enablement rejection.

Claims 24-33 have been canceled. Therefore, this rejection is rendered moot.

Applicants submit that the specification would enable a person of ordinary skill in the art to make and use the macrocyclic tethered tripeptides recited in claims 35 and 36. No further information beyond that disclosed in the instant specification would be required by those skilled in the art in order to make and use the compounds called for in claims 35-37.

The eight factors set forth in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir.1988) further support Applicants' assertion that the enablement requirements are satisfied with respect to claims 35-37, several of which are discussed below:

(1-2) Breadth of claims / nature of invention: The breadth of the claims (and the nature of the claimed invention) has been restricted to macrocyclic tethered tripeptides having particular amino acid side chains and tethers set forth in the claim. These amino acid side chains and tethers are supported by the specification as discussed above. The claimed compounds are similar in structure, all having the three amino acid side chains {W:\06670\000H748-000\00080988.DOC *06670000H748-000* }

and a tether component according to the general formula of claims 35 and 36.

(4) level of ordinary skill: Given the disclosure in the specification regarding the particular compound structures (in both text and structural drawing format), the methods of preparing these particular compounds, and the particularly claimed substituents, a person of ordinary skill in the art would have all of the information needed to make and use the compounds of claims 35 and 36.

(6-7) Amount of direction provided by inventor / existence of working examples:

The Examiner acknowledges (on page 11 of the Final Office Action) that examples of RGD analogs are provided in the specification. RGD analogs are examples of tethered tripeptides, to which claims 35 and 36 are limited. As discussed above, representative examples of tethered tripeptides are provided in the Tables and the text of the specification. These examples cover a representative cross-section of the compounds of claims 35 and 36 and, together with the remainder of the specification, provide the guidance that would be required to enable one of ordinary skill to make and use the compounds of claims 35 and 36. In summary, the specification contains all of the information required to enable a person of ordinary skill in the art to make and use the claimed invention.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 24-33 have been rejected under 35 U.S.C. § 112, second paragraph, as indefinite. According to the Examiner, these claims were indefinite because it was unclear to the Examiner at what position the side chain groups were covalently attached to the macrocyclic compound, and how the bivalent radicals were covalently attached to the macrocyclic compound.

Claims 24-33 have been canceled. Therefore, this rejection is rendered moot.

Regarding claims 35-37, Applicants submit that the position of attachment to the macrocyclic compound is clearly identified with respect to all side chain groups and tethers.

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Other Claim Rejections / Objections

Claims 24-33 have been objected to as requiring correction of informalities; under 35 U.S.C. § 112, first paragraph, as containing subject matter not supported by the specification because, according to the Examiner, these claims contain new matter; and under 35 U.S.C. § 112, second paragraph, as indefinite. Claims 24-33 have been canceled. Therefore, these objections and rejections are rendered moot and are not applicable to new claims 35-37.

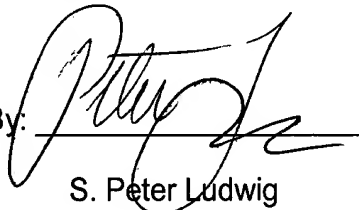
Conclusion

In view of the above amendments and remarks, this application is believed to be in condition for allowance and such action is earnestly solicited.

If there are any other issues remaining, which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,

Dated: November 3, 2003

By: 

S. Peter Ludwig

Reg. No. 25,351


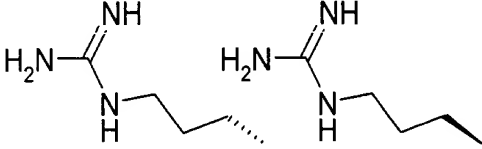
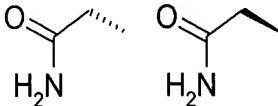
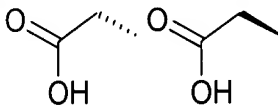

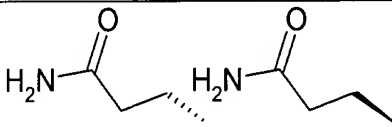
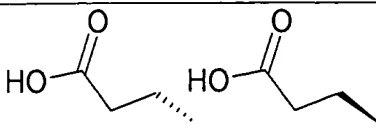
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
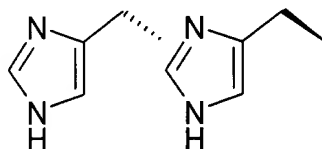
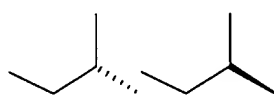
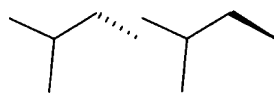
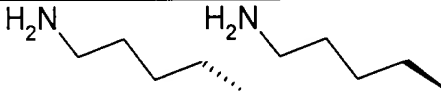

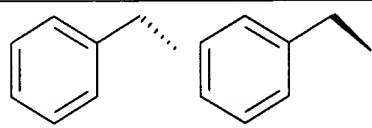
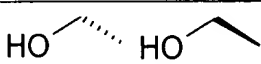
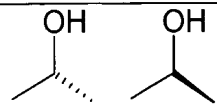
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TABLE A

Amino Acids Side Chains

| R1, R2 or R3 | Support in Specification |
|---|--|
|  | <p>Page 6: shown explicitly as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Figure 1</p> |
|  | <p>Page 6: shown as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Figure 1 (where PGN₁ and PGN₂ are -H)</p> |
|  | <p>Page 6: shown as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Page 7: R₈ is -NH₂</p> <p>Figure 1 (where PGacid is -NH₂)</p> |
|  | <p>Page 6: shown as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Page 7: R₈ is -OH</p> <p>Figure 1 (where PGacid is -OH)</p> |
|  | <p>Page 6: shown as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Page 7: R₉ is -H</p> <p>Figure 1</p> |
|  | <p>Page 6: shown as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Page 7: R₈ is -NH₂</p> <p>Figure 1 (where PGacid is -NH₂)</p> |
|  | <p>Page 6: shown as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Page 7: R₈ is -OH</p> <p>Figure 1 (where PGacid is -OH)</p> |

| R1, R2 or R3 | Support in Specification |
|---|--|
|  | <p>Page 6: shown explicitly as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Figure 1</p> |
|  | <p>Page 6: shown as an option for R₀, R₁, R₂, R₃ and R₄ (where R₅ is -H)</p> <p>Figure 1 (where PGN is -H)</p> |
|  | <p>Page 6: shown explicitly as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Figure 1</p> |
|  | <p>Page 6: shown explicitly as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Figure 1</p> |
|  | <p>Page 6: shown as an option for R₀, R₁, R₂, R₃ and R₄ (where R₅ is -H)</p> <p>Figure 1 (where PGN is -H)</p> |
|  | <p>Page 6: shown explicitly as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Figure 1</p> |
|  | <p>Page 6: shown explicitly as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Figure 1</p> |
|  | <p>Page 6: shown as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Page 7: Figure 1 (R₇ is -H)</p> <p>Figure 1 (where PGO is -H)</p> |
|  | <p>Page 6: shown as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Page 7: Figure 1 (R₇ is -H)</p> <p>Figure 1 (where PGO is -H)</p> |

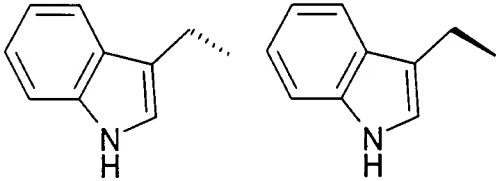
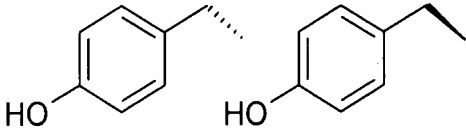
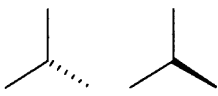

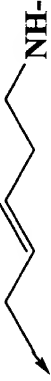


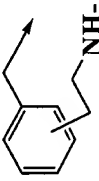
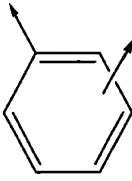
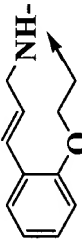
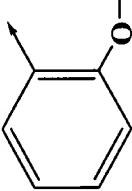

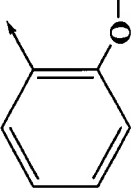

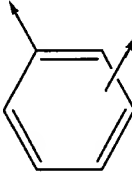
| R1, R2 or R3 | Support in Specification |
|---|--|
|  | <p>Page 6: shown explicitly as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Figure 1</p> |
|  | <p>Page 6: shown as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Page 7: Figure 1 (R₇ is -H)</p> <p>Figure 1 (where PGO is -H)</p> |
|  | <p>Page 6: shown explicitly as an option for R₀, R₁, R₂, R₃ and R₄</p> <p>Figure 1</p> |
| <i>D,L</i> -proline | Figure 1 |
| <i>D,L</i> -4-hydroxyproline | Figure 1 |
| Ornithine | Referenced in original claim 12 as being used as a surrogate for arginine. |
| β-Alanine and γ-Butyric acid | <p>Page 4: contained within the basic definition for the building block elements listed as X-N-(CH₂)_x-CHR₁-C=O (where x is 0 (α-amino acid), 1 (β-amino acid), or 2 (γ-amino acid)).</p> <p>β-Alanine: where R₁, R₂, R₃ or R₄ is -H, and x is 1.</p> <p>γ-Butyric acid: where R₁, R₂, R₃ or R₄ is -H, and x is 2.</p> |

TABLE B

Tethers

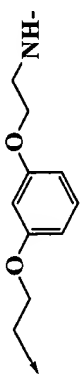
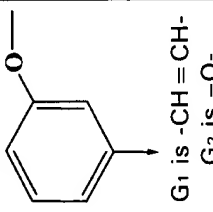
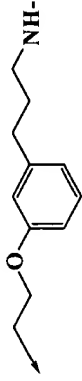
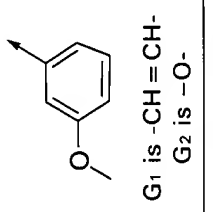
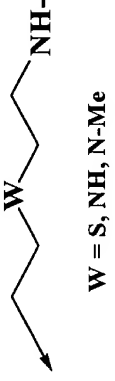
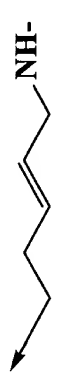

| Tether (T) | (Y) | (L) | | | | (Z) | Support in Specification |
|--|-----------------|---------------------------------|-------|----------------------------------|------|---------------------------------|--|
| | | (CH ₂) _d | A | (CH ₂) _{ij} | B | (CH ₂) _e | |
| The arrow indicates the site of a covalent bond to the nitrogen atom of A ₁ of formula (1) and (-) indicates the site of a covalent bond to the carbonyl carbon of A ₃ of formula (1). | | | | | | | |
|  | CH ₂ | 1 | O | 0 | none | 2 | Page 8, lines 1-5 and original claim 1 (page 48, lines 24-29) |
|  | CH ₂ | 0 | CH=CH | 0 | none | 2 | Page 25: Table 1 Pages 35-37: Tables 4-6 Page 38, lines 9-10 Page 39, line 25 to page 41, line 12 Original claim 10 (page 53) discloses a compound wherein d=0 |
|  | CH ₂ | 1 | CH=CH | 0 | none | 2 | Figure 1 |
|  | CH ₂ | 1 | C≡C | 0 | none | 2 | Figure 1 |

| Tether (T) | (Y) | (L) | | | | | (Z) | Support in Specification |
|---|-----------------|---------------------------------|--|---------------------------------|-------|---------------------------------|-----|--|
| | | (CH ₂) _d | A | (CH ₂) _i | B | (CH ₂) _e | | |
|  meta, para | CH ₂ | 0 |  G ₁ is -CH=CH- No G ₂ | 0 | none | 2 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) Original claim 10 (page 53) discloses a compound wherein d = 0 |
|  | CH ₂ | 1 |  G ₁ is -CH=CH- G ₂ is -O- | 0 | CH=CH | 1 | NH | Page 8, line 1 to page 9, line 5; original claim 1 (page 48, line 24 to page 49, line 29) Figure 1 Page 25: Table 1 Pages 35-37: Tables 4-6 Page 34, lines 14-15 |
|  | CH ₂ | 1 |  G ₁ is -CH=CH- G ₂ is -O- | 0 | none | 3 | NH | Page 8, line 1 to page 9, line 5; original claim 1 (page 48, line 24 to page 49, line 29) Figure 1 |
|  meta, para | CH ₂ | 0 |  G ₁ is -CH=CH- No G ₂ | 0 | none | 2 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) Original claim 10 (page 53) discloses a compound wherein d = 0 |

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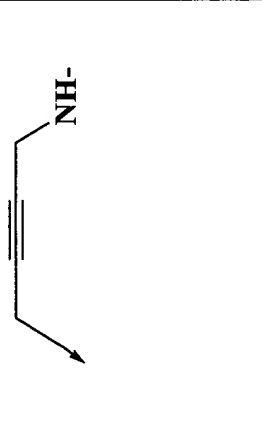
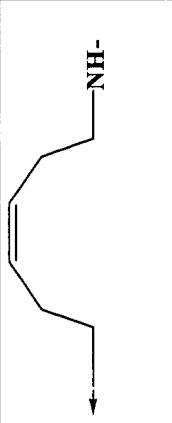
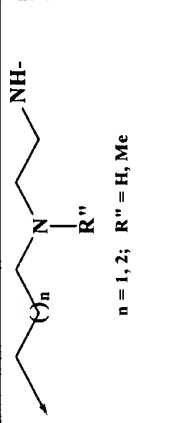
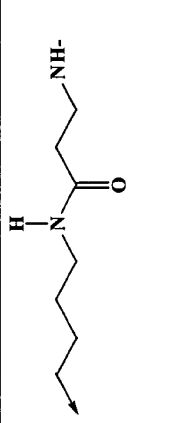
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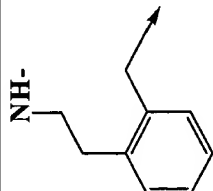
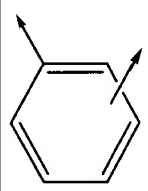
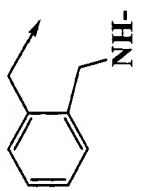
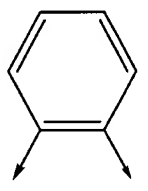
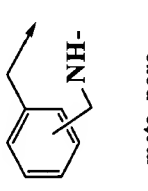
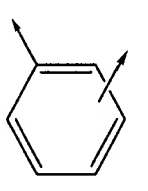
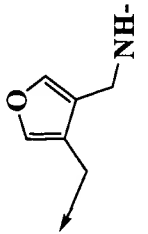
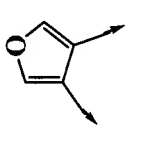
| Tether (T) | (Y) | (L) | | | | | (Z) | Support in Specification |
|--|-----------------|---------------------------------|---|---------------------------------|------|---------------------------------|-----|---|
| | | (CH ₂) _d | A | (CH ₂) _j | B | (CH ₂) _e | | |
|  | CH ₂ | 1 |  G ₁ is -CH=CH- G ₂ is -O- | 0 | 0 | 2 | NH | Page 8, line 1 to page 9, line 5; original claim 1 (page 48, line 24 to page 49, line 29) |
|  | CH ₂ | 1 |  G ₁ is -CH=CH- G ₂ is -O- | 0 | none | 3 | NH | Page 8, line 1 to page 9, line 5; original claim 1 (page 48, line 24 to page 49, line 29) Figure 1 |
|  W = S, NH, N-Me | CH ₂ | 1 | S, NH, N-Me R is Me for the latter | 0 | none | 2 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) |
|  | CH ₂ | 1 | CH=CH | 0 | none | 1 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) Figure 1 |
|  | CH ₂ | 0 | CH=CH | 0 | none | 1 | NH | Page 25: Table 1 Pages 35-37: Tables 4-6 Page 38, lines 6-8 Page 39, lines 20-24 Original claim 10 (page 53) discloses a compound wherein d = 0 |

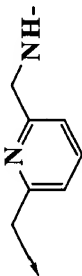
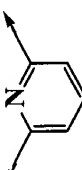
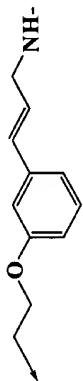
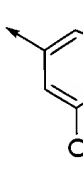
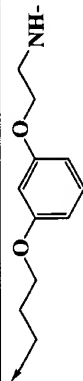
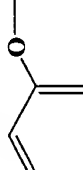
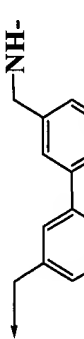
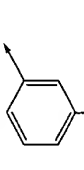
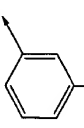
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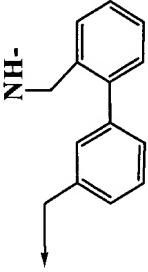
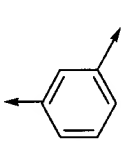
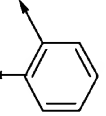
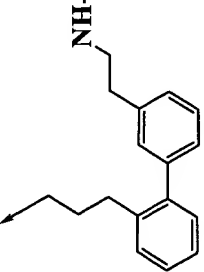
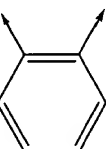
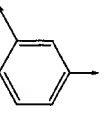
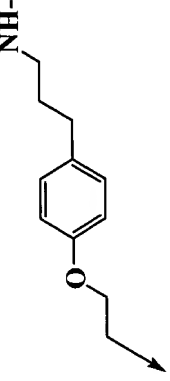
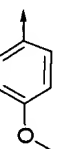
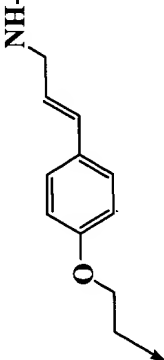
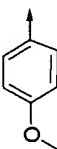
Serial No. 09/679,331

Docket No. 6670/H748
Page 3

| Tether (T) | (Y) | (L) | | | | | (Z) | Support in Specification |
|--|-----------------|---------------------------------|-------------------------------------|---------------------------------|------|---------------------------------|-----|--|
| | | (CH ₂) _d | A | (CH ₂) _j | B | (CH ₂) _e | | |
|  | CH ₂ | 0 | C≡C | 0 | none | 1 | NH | Page 27: Table 3 Page 38, lines 8-9 Page 38, line 13 to page 39, line 19 Original claim 10 (page 53) discloses a compound wherein d = 0 |
|  | CH ₂ | 1 | CH=CH | 0 | none | 2 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) Figure 1 |
|  n = 1, 2; R'' = H, Me | CH ₂ | 2,3 | N-H, N-Me R is Me for the latter | 0 | none | 2 | NH | Page 8, lines 1-9 and original claim 1 (page 48, line 24 to page 49, line 29) |
|  | CH ₂ | 3 | N-H | 0 | C=O | 2 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) |

| Tether (T) | (Y) | (L) | | | | | (Z) | Support in Specification |
|---|-----------------|---------------------------------|---|---------------------------------|------|---------------------------------|-----|--|
| | | (CH ₂) _d | A | (CH ₂) _j | B | (CH ₂) _e | | |
|  | CH ₂ | 0 |  G ₁ is -CH=CH- No G ₂ | 0 | none | 2 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) Original claim 10 (page 53) discloses a compound wherein d = 0 |
|  | CH ₂ | 0 |  G ₁ is -CH=CH- No G ₂ | 0 | none | 1 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) Original claim 10 (page 53) discloses a compound wherein d = 0 |
|  meta, para | CH ₂ | 0 |  G ₁ is -CH=CH- No G ₂ | 0 | none | 1 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) Original claim 10 (page 53) discloses a compound wherein d = 0 |
|  | CH ₂ | 0 |  G ₁ is -O- No G ₂ | 0 | none | 1 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) Original claim 10 (page 53) discloses a compound wherein d = 0 |

| Tether (T) | (Y) | (L) | | | | | (Z) | Support in Specification |
|---|-----------------|---------------------------------|---|---------------------------------|--|---------------------------------|-----|--|
| | | (CH ₂) _d | A | (CH ₂) _j | B | (CH ₂) _e | | |
|  | CH ₂ | 0 |  G ₁ is -CH=N- No G ₂ | 0 | none | 1 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) Original claim 10 (page 53) discloses a compound wherein d = 0 |
|  | CH ₂ | 1 |  G ₁ is -CH=CH- G ₂ is -O- | 0 | CH=CH | 1 | NH | Page 8, line 1 to page 9, line 5; original claim 1 (page 48, line 24 to page 49, line 29) Figure 1 |
|  | CH ₂ | 2 |  G ₁ is -CH=CH- G ₂ is -O- | 0 | 0 | 2 | NH | Page 8, line 1 to page 9, line 5; original claim 1 (page 48, line 24 to page 49, line 29) |
|  | CH ₂ | 0 |  G ₁ is -CH=CH- No G ₂ | 0 |  G ₁ is -CH=CH- No G ₂ | 1 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) Original claim 10 (page 53) discloses a compound wherein d = 0 |

| Tether (T) | (Y) | (L) | | | | | (Z) | Support in Specification |
|---|-----------------|---------------------------------|---|---------------------------------|---|---------------------------------|-----|--|
| | | (CH ₂) _d | A | (CH ₂) _j | B | (CH ₂) _e | | |
|  | CH ₂ | 0 |  G ₁ is -CH=CH- No G ₂ | 0 |  G ₁ is -CH=CH- No G ₂ | 1 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) Original claim 10 (page 53) discloses a compound wherein d = 0 |
|  | CH ₂ | 2 |  G ₁ is -CH=CH- No G ₂ | 0 |  G ₁ is -CH=CH- No G ₂ | 2 | NH | Page 8, lines 1-30 and original claim 1 (page 48, line 24 to page 49, line 29) |
|  | CH ₂ | 1 |  G ₁ is -CH=CH- G ₂ is -O- | 0 | none | 3 | NH | Page 8, line 1 to page 9, line 5; original claim 1 (page 48, line 24 to page 49, line 29) |
|  | CH ₂ | 1 |  G ₁ is -CH=CH- G ₂ is -O- | 0 | CH=CH | 1 | NH | Page 8, line 1 to page 9, line 5; original claim 1 (page 48, line 24 to page 49, line 29) |

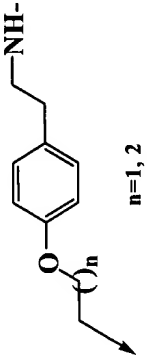
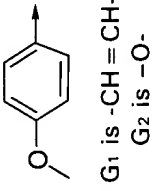
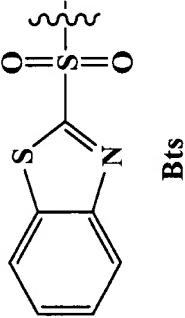
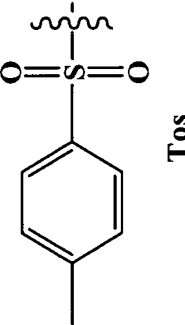
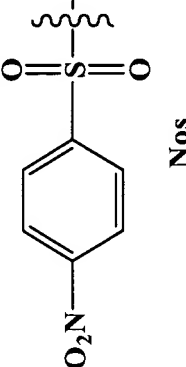
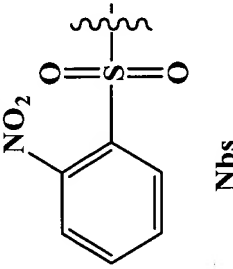
| Tether (T) | (Y) | (L) | | | | (Z) | Support in Specification |
|---|-----------------|---------------------------------|---|---------------------------------|------|-----|---|
| | | (CH ₂) _d | A | (CH ₂) _j | B | | |
|  $n=1, 2$ | CH ₂ | 1, 2 |  G_1 is -CH=CH- G_2 is -O- | 0 | none | 2 | Page 8, line 1 to page 9, line 5; original claim 1 (page 48, line 24 to page 49, line 29) |

Table C
Y Radicals

| Substituent Group with Structure | Support in Document |
|--|--|
|  <p style="text-align: center;">Bts</p> | <p>Specified as part of definition of X, p 5, lines 15-20, also within Claim 1 and Figure 1. Listed as part of the products (denoted simply as B) obtained in Example 1 as presented in Table 1 (p 25), Table 2 (p 26), and Table 3 (p 27). Also as part of the products obtained from Example 4 as presented in Table 4 (p 35, again denoted B) and Example 5 as presented in Table 5 (p 36). Preparation of the Bts amino acid building blocks is presented on pp 42-43.</p> |
|  <p style="text-align: center;">Tos</p> | <p>Part of definition of X, p 5, line 11, also within Claim 1 and Figure 1, as generic -SO₂Ar, where Ar is a substituted aromatic group, in this case tolyl.</p> |
|  <p style="text-align: center;">Nos</p> | <p>Part of definition of X, p 5, line 11, also within Claim 1 and Figure 1, as generic -SO₂Ar, where Ar is a substituted aromatic group, in this case 4-nitrophenyl.</p> |
|  <p style="text-align: center;">Nbs</p> | <p>Part of definition of X, p 5, line 11, also within Claim 1 and Figure 1 as generic -SO₂Ar, where Ar is a substituted aromatic group, in this case 2-nitrophenyl.</p> |

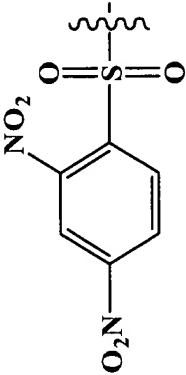
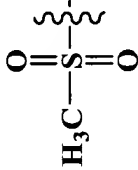
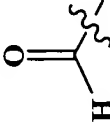
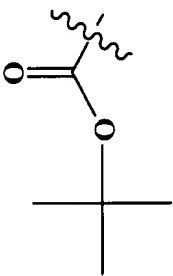
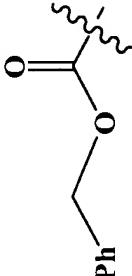




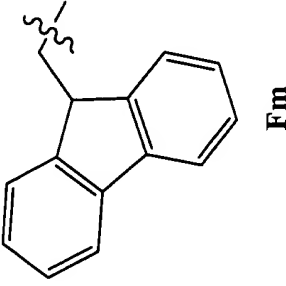
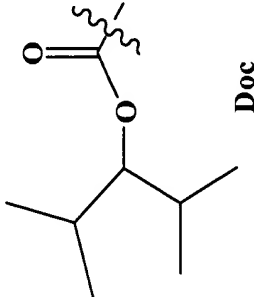
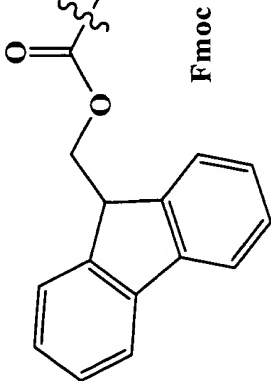
| | |
|--|---|
|  <p style="text-align: center;">Dnps</p> | <p>Part of definition of X, p 5, line 11, also within Claim 1 and Figure 1 as generic -SO₂Ar, where Ar is a substituted aromatic group, in this case 2,4-dinitrophenyl.</p> |
|  <p style="text-align: center;">Ms</p> | <p>Specified as part of definition of X, p 5, line 11, also within Claim 1 and Figure 1. Listed as part of the products obtained in Example 6 as presented in Table 6 (p 37).</p> |
|  <p style="text-align: center;">Formyl</p> | <p>Specified as part of definition of X, p 5, line 11, also within Claim 1 and Figure 1, written as COH instead of the more common CHO abbreviation. Preparation of three compounds containing this moiety presented as Example 3 (pp 31-32).</p> |

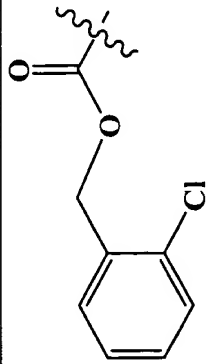
Table D

Protecting Groups on Amino Acids side chains (W)

| Substituent Group with Structure | Support in Document |
|---|---|
|  <p style="text-align: center;">Boc</p> | <p>Specified as part of definition of R₆₁ and R₆₂, p 6, line 23, also within Claim 1. Specified in Figure 1 as part of definition of PGN where PGN₁ and PGN₂ are shown on the Arg side chain.</p> <p>Specified as part of definition of R₅, p 6, line 23, also within Claim 1, with R₅ being -COO-tBu. Specified in Figure 1 as part of definition of PGN.</p> |
|  <p style="text-align: center;">Cbz</p> | <p>Part of definition of R₆₁ and R₆₂, p 6, line 23, also within Claim 1, as -COO-CH₂-Ar where Ar, the aromatic moiety, is phenyl. Specified in Figure 1 as part of definition of PGN (PGN₁ and PGN₂ are shown on the Arg side chain), where it is listed as -CO-O-Bn, with Bn being an acceptable alternative abbreviation for benzyl.</p> <p>Part of definition of R₅, p 6, line 23, also within Claim 1, with R₅ being -COO-CH₂-Ar with Ar, an aromatic moiety, being phenyl. Specified in Figure 1 as part of definition of PGN as -CO-O-Bn where Bn is an acceptable alternative abbreviation for benzyl.</p> <p>Specified as part of definition of R₈, p 7, line 11, also within Claim 1, with R₈ being -O-tBu. Specified in Figure 1 as part of definition of PGacid as -O-tBu.</p> |
|  <p style="text-align: center;">tBu</p> | <p>Specified as part of definition of R₈, p 7, line 19, also within Claim 1, with R₉ being -tBu. Specified as part of definition of PGS in Figure 1.</p> |
|  <p style="text-align: center;">Bzl</p> | <p>Part of definition of R₈, p 7, line 12, also within Claim 1, with R₈ as -O-CH₂-Ar with Ar, an aromatic moiety, being phenyl. Specified in Figure 1 as part of definition of PGacid as -O-Bn, with Bn being an acceptable alternative abbreviation for benzyl.</p> |

| | |
|---|--|
|  | Specified as part of definition of R ₈ , p 7, line 11, also within Claim 1, with R ₈ being -OCH ₃ . Specified in Figure 1 as part of definition of PGacid as -OCH ₃ . Listed as part of the products obtained in Example 6, p 37. |
|  | Part of definition of R ₈ , p 7, line 12, also within Claim 1, with R ₈ as -O-CH ₃ substituted with the selection of -CH ₃ from the specified group presented. Part of definition of PGacid in Figure 1 with PGacid being -O-CH ₃ substituted with the selection of -CH ₃ from the specified group listed in the footnote. |
|  | Part of definition of R ₈ , p 7, line 12, also within Claim 1, with R ₈ being -O-CH ₂ -Ar with Ar, an aromatic moiety, being fluorenyl. |
|  | Specifically presented within Example 1 (p 20) as well as in an Example preparation of N ^α -Boc-N ^m -Doc-histidine as an amino acid building block on pp 41-42. |
|  | Part of definition of R ₅ , p 6, line 23, also within Claim 1, with R ₅ being -COO-CH ₂ -Ar with Ar, an aromatic moiety, being fluorenyl. |

Part of definition of R₅, p 6, line 23, also within Claim 1, with R₅ being -COO-CH₂-Ar with Ar, an aromatic moiety, being 2-chlorophenyl.



2-Cl-Z